Introduction
Activation of p53 by blocking the p53-Mdm2 interaction using non-peptidic small-molecule inhibitors is being pursued as a promising cancer therapeutic strategy. In the present study, we show the identification of NVP-CGM097, a novel, highly optimized, and selective inhibitor of the p53-Mdm2 interaction. The validation and understanding of its mechanism of action, the overall favorable drug-like properties and the characterization of its on-target toxicological profile in preclinical species strongly supported the initiation of Phase I clinical trials with NVP-CGM097 in pre-selected patients with p53 wild-type tumors.

NVP-CGM097 structure and binding to Mdm2

Cellular profiling of NVP-CGM097 (cont')

2. Cancer Cell Line Encyclopedia: CGM097 sensitivity profile

p53WT status is necessary but not sufficient for cells to be sensitive to NVP-CGM097

NVP-CGM097 induces a specific p53-dependent anti-proliferative effect

NVP-CGM097 triggers rapid and sustained activation of p53-dependent PD biomarkers resulting in tumor regression of the p53WT and Mdm2-amplified SJSA-1 xenograft model in mice

Conclusions
- NVP-CGM097 is a potent and selective p53-Mdm2 inhibitor
- NVP-CGM097 induces p53-dependent anti-proliferative effects
- NVP-CGM097 has a desirable PK profile across species, and a good PK/PD relationship in vivo
- NVP-CGM097 induces p53-dependent tumor regression in SJSA-1 xenograft models at well tolerated doses
- NVP-CGM097 is being tested in Phase I clinical trials in patients with p53WT solid tumors

Presented at the AACR 2014 Annual Meeting; 5-9 April 2014; San Diego, CA.